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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,481	02/27/2002	Hiroaki Takayama	TAKAYAMA10	3430

1444 7590 09/24/2003

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EXAMINER
QAZI, SABIHA NAIM

ART UNIT	PAPER NUMBER
1616	12

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/069,481	Applicant(s) TAKAYAMA ET AL.	
	Examiner Sabiha Qazi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *01 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-3,6 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-3, 6 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Invention: *The instant invention is drawn to 2-substituted vitamin D_3 derivative, their composition and method of use.*

Acknowledgement is made of the response, amendments and request for reconsideration filed on 7/1/03. Claims 1-3, 6 and 7 are pending and rejected. No claim is allowed. Amendments are entered.

Rejections under second and first paragraph of 35 U.S.C. 112 are withdrawn because claims are amended. Arguments were fully considered but are not found persuasive therefore; all the rejections are maintained for the same reasons as set forth in our previous office action.

The basis of the argument is that alpha substituted compounds are better than beta, which is not convincing because alpha is disclosed and taught by the prior art of record. Prior art teaches that 2-alpha substituted vitamin D3 is better than beta.

Even though claims are amended claimed invention is not considered allowable over the prior art for the same reasons as set forth in our previous office action.

The argument that there is no motivation to prepare alpha isomer is not convincing because when the invention was made it was known to one skilled in the art that 2-alpha methyl vitamin D3 (aab and aaa) isomers compounds showed much higher potency than the corresponding 2beta methyl isomers (abb and aba). See Fujishima et al and Konno et al.

It is unclear to the examiner what is the criticality of the invention when the invention as claimed is already disclosed and taught by the references.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

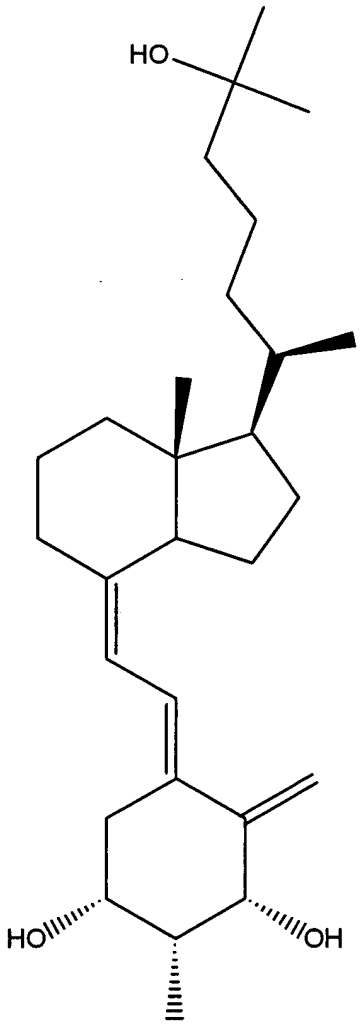
A person shall be entitled to a patent unless –

1. Claims 1-3, 6 and 7 stand rejected under 35 U.S.C. 102(b) as being anticipated by Konno et al. (Bioorganic & and Medicinal Chemistry Letters 8 (1998) 151-156 and Fujishima et al. (Bioorganic & and Medicinal Chemistry Letters, (1998), 2145-2148). In Konno reference see compound Table I and Ist Para on page 154. See compound 4 on page 155. Note that compound having 2-alpha substitutions is better than the beta position. See compound 3 on page 2145 and compound 4 on page 2146 in Fujishima et al.

1. Claims 1-3, 6 and 7 stand rejected under 35 U.S.C. 102(b) as being anticipated by Posner et al. (WO 96/01811). See compound 3 on page 4, which is the same as presently claimed.

1. Claim 1, 2, 3 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Konno et al. (Bioorganic & and Medicinal Chemistry Letters

8 (1998) 151-156) and Fujishima et al. (Bioorganic & and Medicinal Chemistry Letters, (1998), 2145-2148). See the entire documents especially In Konno reference see compound Table I and lines Ist para on page 154. See compound 4 on page 155. See compound 3 on page 2145 and compound 4 on page 2146 in Fujishima et al.



2alpha-methyl-1alpha,25-dihydroxyvitamin D3

These references disclose that 20-epi-alpha-alpha-beta analogue exhibited 12-fold higher affinity than 1-alpha, 25-dihydroxyvitamin D3, whereas alpha-beta-

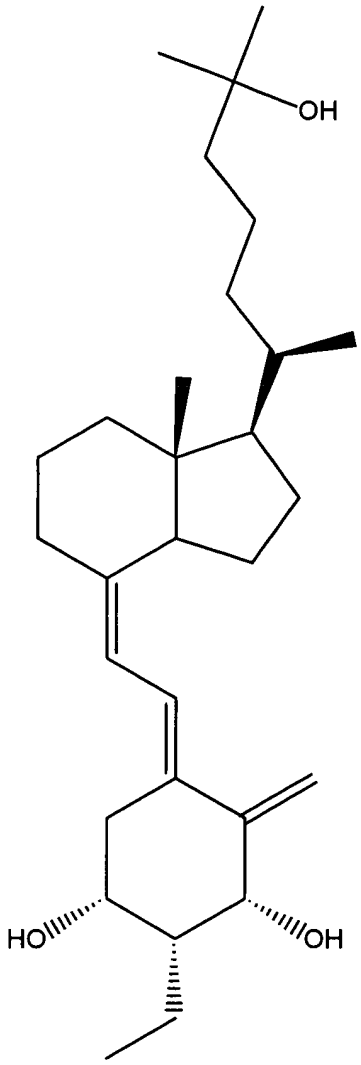
beta has comparable activity to 1-alpha, 25-dihydroxyvitamin D3. See second Para and Table 1on page 2147 of Fujishima reference.

Presently claimed invention differs from the reference in that they are of different generic scope. It had been held by Courts that the indiscriminate selection of "some" from among "many" is considered prima facie obvious. In re Lemin, 141 USPQ 814 (1964); National Distillers and Chem. Corp. V. Brenner, 156 USPQ 163.

The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare compounds embraced by the genus of the above cited references with the expectation of obtaining additional beneficial compounds useful as antitumor agents, an immunomodulator etc.

One having ordinary skill in the art would be motivated to prepare additional derivatives of vitamin D_3 because prior art teaches 2-substituted vitamin D derivatives for various uses. It would have been obvious who is even familiar with the art at the time of invention to prepare the compounds and compositions for various uses as instantly claimed.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).



2alpha-ethyl-1alpha,25-dihydroxyvitamin D3

This 2-alpha ethyl, compound of present invention is a homolog of the prior art (Konno and Fujishima) compound.

The prior art of record is drawn to structurally similar compounds, which differ, from the compounds embraced by the instant claims in that they are homologs. The skilled artisan would have been motivated to modify the teaching of the prior art to prepare homologs because it is recognized in the art

that homologs are structurally similar and would be expected to possess similar properties. *Ex parte Henze* (POBA 1948) 83 USPQ 167 .

Compounds that differ only by the presence of an extra methyl group are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders prima facie obvious its homologue.

The homologue is expected to be prepare able by the same method and to have the same properties i.e. useful as antidiabetic agent.

This expectation is then deemed the motivation for preparing homologues. The homologues are obvious even in the absence of a specific teaching to methylate, *In re Wood* 199 USPQ 137; *In re Hoke* 195 USPQ 148; *In re Lohr* 137 USPQ 548; *In re Magerlein* 202 USPQ 473; *In re Wiechert* 152 USPQ 249; *Ex parte Henkel* 130 USPQ 474; *In re Fauque* 121 USPQ 425; *In re Druey* 138 USPQ 39.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438,

164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 3, 6 and 7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 3 claims of co pending Application No. 09/214,155 and claims 1-3, 5-8 and 10-13 of 09/959,541 respectively. Although the conflicting claims are not identical, they are not patentably distinct from each other because 2-position of vitamin D represents lower alkyl group and it is claimed in 10/069,481. In claim 1 of 09/214,155 a methyl group at alpha and beta position is claimed at 2- position, which is considered obvious because a methyl group is included in lower alkyl group. In 10/069,481 vitamin D3 is 2-substituted alkyl. In all the above copending applications and presently

claimed invention 2-substituted vitamin D3 compounds are claimed which are considered obvious over the other.

Applicants must disclose all the copending and any patent related to this application.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is 703-305-3910. The examiner can normally be reached on every business day..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The

fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

S. Qazi

SABIHA QAZI, PH.D
PRIMARY EXAMINER